Claims:

1. A nucleic acid molecule comprising a $P66^{shc}$ coding sequence incorporating at least one mutation as compared to the wild type sequence or the sequence as shown in Fig. 5 such that the protein encoded by the coding sequence has at least one serine residue absent or replaced by a different amino acid residue.

2. A nucleic acid molecule according to claim 1 wherein the serine residue is selected from the group S17, S19, S20, S26, S28, S36, S38, S40, S41, S54, S60, S66, S80 or S120.

3. A nucleic acid molecule according to claim 1 or claim 2 wherein the serine residue is selected from the group S28, S36 and S54.

4. A nucleic acid molecule according to any one of the preceding claims wherein the serine residue is S36 and is replaced by alanine ($p66^{shc}S36A$)

5. A polypeptide encoded by a nucleic acid molecule according to any one of the preceding claims.

6. A replicable vector comprising nucleic acid according to any one of claims 1 to 4 operably linked to control sequences to directs its expression.

7. A host cell transformed with a vector according to claim 6.

8. A method of producing a modified $p66^{Shc}$ polypeptide comprising culturing a host cell according to claim 7 so

that the $p66^{shc}$ polypeptide is produced.

9. A method of affecting the $p66^{shc}$ signal transduction pathway in a cell, said method comprising the step of contacting said cell with an agent capable of modulating $p66^{shc}$ gene expression.

10. A method according to claim 9 wherein said agent is a nucleic acid molecule capable of hybridizing to nucleic acid encoding $p66^{shc}$ thereby reducing or preventing said $p66^{shc}$ thereby reducing or preventing said $p66^{shc}$ expression.

11. A method according to claim 9 wherein said agent is a vector comprising nucleic acid encoding $p66^{shc}$, said vector being capable of incorporating said nucleic acid into the genome of the cell so that the nucleic acid encoding $p66^{shc}$ is expressed in the cell.

12. A method of increasing resistance in cells to oxidative stress comprising the step of disrupting the $p66^{shc}$ signalling pathway.

13. A method according to claim 12 wherein said step of disrupting the $p66^{shc}$ effects the susceptibility of $p66^{shc}$ to phosphorylation.

14. A method according to claim 12 or claim 13 wherein said step of disrupting the $p66^{shc}$ pathway causes a mutant $p66^{shc}$ polypeptide to be expressed such that at least one serine residue present in the wild type $p66^{shc}$ is absent or replaced by a different amino acid residue.

15. A method according to claim 14 wherein said serine

residue is S36 and is replaced by alanine

16. A method according to claim 14 wherein said mutant polypeptide cannot be serine phosphorylated.

17. A method according to any one of claims 12 to 16 wherein said disruption effects the ability of a serine/threonine kinase, p38 or MAPK to phosphorylate $p66^{shc}$.

18. A method according to claim 12 wherein the step of disrupting the $p66^{shc}$ signalling pathway includes contacting the cell with an antibody binding domain capable of specifically binding to the $p66^{shc}$ polypeptide such that its function is disrupted or prevented.

19. A method according to claim 12 wherein said step of disrupting the $p66^{shc}$ signalling pathway includes disrupting the $p66^{shc}$ gene expression.

20. A method according to claim 19 wherein disruption of the $p66^{shc}$ gene expression includes contacting the cell with a substance capable of interfering with the expression of nucleic acid encoding the $p66^{shc}$ polypeptide so as to reduce or prevent its production.

21. A method according to claim 20 wherein the substance is an antisense oligonucleotide capable of hybridising to the nucleic acid encoding the $p66^{shc}$ polypeptide.

22. Use of a substance which disrupts $p66^{shc}$ or a step in the $p66^{shc}$ signalling pathway, in the preparation of a medicament to increase cellular resistance to oxidative stress.

23. Use of an antisense oligonucleotide capable of specifically hybridising to p66^{shc} nucleic acid in the preparation of a medicament for increasing resistance in cells to oxidative stress.

24. Use according to claim 23 wherein said antisense oligonucleotide is RNA

25. Use according to claim 23 or claim 24 wherein the p66^{shc} nucleic acid sequence is shown in Fig. 5.

26. Use of an antibody binding domain capable of specifically binding to a p66^{shc} polypeptide or fragment thereof in the preparation of a medicament for increasing resistance in cells to oxidative stress.

27. Use according to any one of claims 22 to 26 wherein the medicament is for the treatment of diseases including lung emphysema, myocardial infarction, stroke, premature aging, cell senescence, Parkinson's, Alzheimer, cancers and diabetes.

28. A method of increasing resistance to tumour formation in a tissue comprising the step of increasing the expression of p66^{shc} in said tissue.

29. A method according to claim 28 wherein the step of increasing the expression of p66^{shc} includes contacting the tissue with an agent capable of increasing expression of p66^{shc} gene.

30. A method according to claim 29 wherein said agent is a transcription factor.

31. A method according to claim 29 wherein said agent is a vector comprising nucleic acid encoding $p66^{shc}$ polypeptide said vector being capable incorporating said nucleic acid into the genome the cells of the tissue.

32. A method of screening for compounds capable of modulating a $p66^{shc}$ signalling pathway comprising contacting a candidate compound with a $p66^{shc}$ expression system; determining the amount of a compound of the signalling pathway; and comparing said amount of the component with the amount of the component in the absence of said candidate compound.

33. A method according to claim 32 further comprising the step of preparing a pharmaceutical composition comprising the candidate compound capable of modulating a $p66^{shc}$ pathway and a pharmaceutical acceptable carrier.

34. A method according to claim 32 or claim 33 wherein said step of determining the amount of a compound of the signalling pathway is an enzyme activity assay.

35. A method according to any one of claims 32 to 34 wherein said candidate compounds include nucleic acid sequences, antibody binding domains, and protein nucleic acids.

36. A method of reducing intracellular levels of reactive oxygen species (ROS) in a cell, said method comprising the step of contacting said cell with an agent capable of inhibiting the expression or activity of $p66^{shc}$ polypeptide.

37. A method according to claim 36 wherein said agent is

a nucleic acid molecule capable of specifically hybridising with nucleic acid with the cell which codes for the $p66^{shc}$ polypeptide such that expression the $p66^{shc}$ polypeptide is reduced or prevented.

38. A method according to claim 36 wherein the agent is an antibody binding domain capable of specifically binding to the $p66^{shc}$ polypeptide such that its functions are inhibited or prevented.

39. Use of an oligonucleotide sequence capable of specifically hybridising to a $p66^{shc}$ nucleic acid coding sequence or fragment thereof for detecting the presence or absence of $p66^{shc}$ nucleic acid in a biological sample.

40. Use according to claim 39 wherein said oligonucleotide is more than 20 nucleotides in length and is derived from the sequence shown in Fig. 5,

41. Use of an antibody binding domain capable of specifically binding to a $p66^{shc}$ polypeptide for detecting the presence or absence of $p66^{shc}$ polypeptide in a biological sample.

42. A method of determining the presence or absence of a $p66^{shc}$ nucleic acid or a mutant, variant derivative or allele thereof in a biological sample, comprising the step of contacting said sample with a nucleic acid molecule capable of hybridising specifically with said $p66^{shc}$ nucleic acid or a mutant, variant derivative or allele thereof and determining whether or not hybridization has taken place.

43. A method of determining the presence or absence of a

p66^{shc} polypeptide or a mutant, variant derivative or allele thereof in a biological sample, comprising the step of contacting said sample with an antibody binding domain capable of hybridising specifically with said p66^{shc} nucleic acid or a mutant, variant derivative or allele thereof and determining whether or not hybridization has taken place.

44. An expression system comprising a nucleic acid vector having a p66^{shc} coding sequence or fragment thereof inserted therein.

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